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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/732,047 | 12/07/2000 | Edwin F. Ullman | BEH-7385 | 9672 |

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EXAMINER

VENCI, DAVID J

| ART UNIT | PAPER NUMBER |
|----------|--------------|
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1641

DATE MAILED: 08/28/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/732,047

Applicant(s)

ULLMAN ET AL.

Examiner

David J. Venci

Art Unit

1641

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on June 12, 2006.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 44-46 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 44-46 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- ☒ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____
- ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- ☐ Notice of Informal Patent Application (PTO-152)
- ☐ Other: _____

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action is withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on March 31, 2006, is entered.

Currently, claims 44-46 are under examination.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Specification

The amendment filed December 2, 2005, is objected to under 35 U.S.C. 132(a) because it introduces new matter into the disclosure. Section 132(a) of 35 U.S.C. states that no amendment shall introduce new matter into the disclosure of the invention. Applicants are required to cancel the new matter in the reply to this Office Action. The added material which is not supported by the original disclosure is as follows:

Amendment to the paragraph on page 4, lines 20-30:

Addition of a linker attaching "substrate molecules to a detectable product"

The amendment filed December 2, 2005, is further objected to because of the following informalities:

Amendment to the paragraph on page 5, lines 1-14:

The mechanism by which "release of the substrate with formation of a first binding site may be accompanied by unmasking of at least some of a second binding site" is mechanistically unclear.

The amendment filed March 31, 2006, is objected to because of the following informalities:

Amendment to the paragraph on page 9, lines 5-22:

The sentence "When peroxide or singlet oxygen is generated, an oxidant cleavable linker is cleaved, releasing the multiple substrates as multiple products" is indefinite. How "multiple substrates" are release as "multiple products" is not clear.

Claim Rejections - 35 USC § 112 – second paragraph

Claims 44-46 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 44:

The pronoun "its" is indefinite. The identity of one or more objects referenced by "its" is not clear. Whether "its" references "second specific binding pair member" AND/OR/NOT "sensitizer" is not clear.

The phrase "releases digoxigenin-linked biotin from the support" is indefinite in view of antecedent phrase "a substrate bound to the support". Whether/how object "digoxigenin-linked biotin" is released from class "substrate" is not clear. Whether/how object "digoxigenin-linked biotin" is released from class "substrate bound to the support" is not clear.¹

The phrase "linked to the support" is indefinite in view of antecedent phrase "bound to the support". The identity of objects and/or steps required for "linking" versus "binding" is not clear. Whether object(s) required for "linking" are co-extensive with object(s) required for "binding" is not clear.²

¹ Applicants may obviate this rejection by deleting all references to a "substrate" in claim 44.

² *Id.*

Claim Rejections - 35 USC § 102

Claims 44-46 are rejected under 35 U.S.C. 102(e) as being anticipated by Bronstein *et al.* (US 6,243,980).

Bronstein *et al.* describe a method for determining the presence or concentration of an analyte in a medium, said method comprising:

(1) providing a reacting mixture comprising in combination:

(a) a medium (see Abstract, first sentence, "sample") suspected of containing an analyte (see Title, "protease inhibitor"; see *also* col. 7, lines 13-14, "the other member of the first pair");

(b) a first specific binding pair member (see Fig. 3, "alkaline phosphatase") bound to a support (see Fig. 3, adamantyl moiety);

(c) a second specific binding pair member (see Fig. 3, OPO_3^-) bound to a sensitizer (see col. 5, line 35, "1,2-dioxetane moiety precursor") capable in its excited state of generating a reactive oxygen species (see col. 5, lines 36-37, "photooxygenated in situ to the dioxetane (14B)"), wherein the proximity of the first specific binding pair member with the second specific binding pair member is modulated by the presence of the analyte (see Abstract, fifth and sixth sentences, "Substrate cleavage, if not inhibited, is allowed to occur, and any unbound cleaved fragments are removed. An enzyme complexed with the second member of the second ligand binding pair is added, and allowed to bind to any of the (uncleaved) first member of the second ligand binding pair remaining");

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(d) a substrate (see Abstract, second sentence, "a peptide bearing a cleavage site for the protease of interest") bound to the support (see Fig. 3, adamantyl moiety), said substrate comprising digoxigenin-linked biotin (see col. 7, lines 10-12, "labels for either end of the peptide are: Biotin... and Digoxin (digoxigenin labeled peptide)") (paraphrasing mine) linked to the support (see Fig. 3, adamantyl moiety) through a reactive oxygen cleavable linker (see Abstract, first sentence, "1,2-dioxetanes");

(2) incubating the reaction mixture (see Abstract, fifth sentence, "Substrate cleavage, if not inhibited, is allowed to occur");

(3) exciting the sensitizer, said excitation of the sensitizer causing the formation of reactive oxygen (see col. 5, lines 36-37, "photooxygenated in situ to the dioxetane (14B)"), which cleaves the cleavable linker and releases digoxigenin-linked biotin from the support (see Fig. 3 and col. 3, lines 6-7, "decomposition"); and

(4) detecting the released digoxigenin-linked biotin, the amount thereof being related to the amount of analyte in said medium (see Abstract, last sentence, "when the dioxetane is caused to decompose, energy is transferred to the fluorescing entity, which releases light of a wavelength recognizably distinct").

Response to Arguments

In prior Office Action, Examiner objected to the amendment filed December 2, 2005, specifically, the amendment to the paragraph on page 5, lines 1-14, because the mechanism by which "release of the substrate with formation of a first binding site may be accompanied by unmasking of at least some of a second binding site" (emphasis mine) is considered mechanistically unclear.

In response, Applicants point to allegedly analogous mechanisms of:

- (1) a substrate linked to a support via a linker, whereupon cleavage of the linker unmask a binding site (see Applicants' reply, p. 9, second full paragraph, second sentence);
- (2) supports having "pores" (see Applicants' reply, p. 9, second full paragraph, fifth sentence);
- (3) specific binding reagents that are "bulky" (see Applicants' reply, p. 9, second full paragraph, sixth sentence); and
- (4) unmasking of biotin (see Applicants' reply, paragraph bridging pp. 9-10).

Applicants' arguments are not persuasive. None of (1) to (4) are analogous to the mechanism as described in the amendment filed December 2, 2005. None of (1) to (4) describe a mechanism involving both: (1) formation of a first binding site; and (2) unmasking of a second binding site.

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Conclusion

No claims are allowed at this time.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Venci whose telephone number is 571-272-2879. The examiner can normally be reached on 08:00 - 16:30 (EST). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

David J Venci
Examiner
Art Unit 1641

djv


CHRISTOPHER L. CHIN
PRIMARY EXAMINER
GROUP 1800 1641
8/21/06